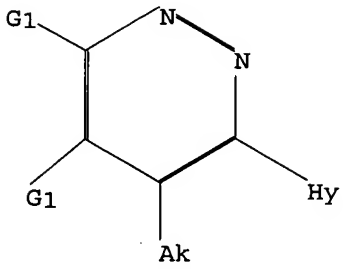

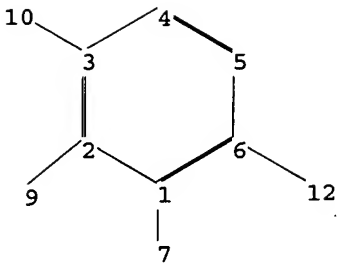

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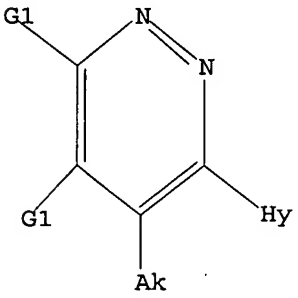
7 9 10 12
ring nodes :
1 2 3 4 5 6
chain bonds :
1-7 2-9 3-10 6-12
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-7 2-9 3-10 6-12
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

G1:Cb,Hy

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 9:CLASS 10:CLASS 12:Atom

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 Cb,Hy

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 16:16:00 FILE 'REGISTRY'

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SAMPLE SCREEN SEARCH COMPLETED -     4642 TO ITERATE

 43.1% PROCESSED     2000 ITERATIONS                                 1 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        88755 TO    96925
PROJECTED ANSWERS:               1 TO      137

L2            1 SEA SSS SAM L1

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FULL SCREEN SEARCH COMPLETED -    90726 TO ITERATE

100.0% PROCESSED    90726 ITERATIONS                                20 ANSWERS
SEARCH TIME: 00.00.01

L3           20 SEA SSS FUL L1

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   166.94     167.15

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FILE LAST UPDATED: 5 Apr 2006  (20060405/ED)

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=> s l3
L4            4 L3

=> d ibib abs hitstr tot
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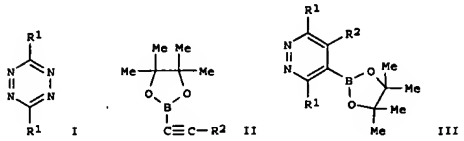
L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:595115 CAPLUS
DOCUMENT NUMBER: 143:248349
TITLE: Synthesis of highly substituted pyridazines through alkynyl boronic ester cycloaddition reactions
AUTHOR(S): Helm, Matthew D.; Moore, Jane E.; Plant, Andrew; Harrity, Joseph P. A.
CORPORATE SOURCE: Department of Chemistry, University of Sheffield, Sheffield, S3 7HF, UK
SOURCE: Angewandte Chemie, International Edition (2005), 44(25), 3889-3892
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

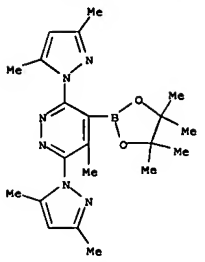


AB A highly regioselective transformation of tetrazines I (R1 = CO2Me, 3,5-dimethylpyrazol-1-yl, H) through a cycloaddn. reaction with alkynyl boronic esters II (R2 = Me, n-Bu, SiMe3, Ph, H) provides highly substituted pyridazine boronic esters III as intermediates for C-O and C-C bond-forming reactions. Functionalization reactions of the C-B bond, such as oxidation and the Suzuki cross-coupling, show the versatility of these species.

IT **863422-36-0P 863422-53-1P 863422-55-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of pyridazines via regioselective cycloaddn. of alkynyl boronic esters with tetrazines and their oxidation and Suzuki cross-coupling reactions)

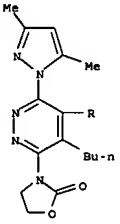
RN 863422-36-0 CAPLUS
CN Pyridazine, 3,6-bis(3,5-dimethyl-1H-pyrazol-1-yl)-4-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)- (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



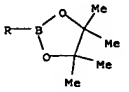
RN 863422-53-1 CAPLUS
CN 2-Oxazolidinone, 3-[4-butyl-6-(3,5-dimethyl-1H-pyrazol-1-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-pyridazinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



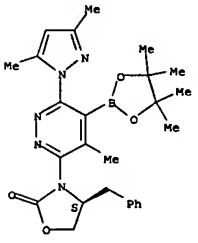
L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 2-A



RN 863422-55-3 CAPLUS
CN 2-Oxazolidinone, 3-[6-(3,5-dimethyl-1H-pyrazol-1-yl)-4-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-pyridazinyl]-4-(phenylmethyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

own work

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:927172 CAPLUS
DOCUMENT NUMBER: 141:395567
TITLE: Preparation of substituted pyridazines and analogs for treatment of TNF-α, IL-1β, IL-6, and/or IL-8 mediated disorders
INVENTOR(S): Dominguez, Celia; Goldberg, Martin H.; Tamayo, Nuria A.
PATENT ASSIGNEE(S): Amgen Inc., USA
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094379	A2	20041104	WO 2004-US11953	20040415
WO 2004094379	A3	20050331		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004254178	A1	20041216	US 2004-826982	20040415
EP 1628665	A2	20060301	EP 2004-750293	20040415
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				

PRIORITY APPLN. INFO.: US 2003-463697P P 20030416
WO 2004-US11953 W 20040415

OTHER SOURCE(S): MARPAT 141:395567
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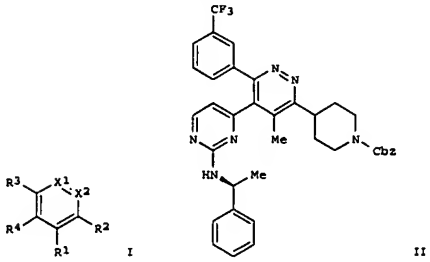
L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



I II

AB Title compds. I [wherein X1, X2 = independently (un)substituted CH, N; with the proviso that at least one of X1 and X2 = N; R1 = (halo)alkyl, CN, NO2, acyl, carboxy, carbamoyl, alkoxy, sulfamoyl, ureido, etc.; R2 = alkyl, Ph, PhCH2, heterocyclyl, etc.; R3, R4 = independently (un)substituted Ph, naphthyl, heterocyclyl; or pharmaceutically acceptable salts thereof] were prepared as TNF-α, IL-1β, IL-6, and/or IL-8 inhibitors. For example, a multi-step synthesis concluding with the reaction of 4-[5-(2-methanesulfonylpyrimidin-4-yl)-4-methyl-6-(3-trifluoromethylphenyl)pyridazin-3-yl]piperidine-1-carboxylic acid benzyl ester and (S)-(-)-1-phenylethylamine gave II. The latter inhibited lipopolysaccharide-activated THP1 cell TNF-α production with IC50 <20 μM. Thus, I and their pharmaceutical compns. are useful for the treatment of inflammation, rheumatoid arthritis, Paget's disease, osteoporosis, multiple myeloma, uveitis, acute or chronic myelogenous leukemia, pancreatic b cell destruction, osteoarthritis, rheumatoid spondylitis, gouty arthritis, inflammatory bowel disease, adult respiratory distress syndrome (ARDS), psoriasis, Crohn's disease, allergic rhinitis, ulcerative colitis, anaphylaxis, contact dermatitis, asthma, muscle degeneration, cachexia, Reiter's syndrome, type I diabetes, type II diabetes, bone resorption diseases, graft vs. host reaction, Alzheimer's disease, stroke, myocardial infarction, ischemia reperfusion injury, atherosclerosis, brain trauma, multiple sclerosis, cerebral malaria, sepsis, septic shock, toxic shock syndrome, fever, myalgias due to HIV-1, HIV-2, HIV-3, cytomegalovirus (CMV), influenza, adenovirus, the herpes viruses, or herpes zoster infection (no data).

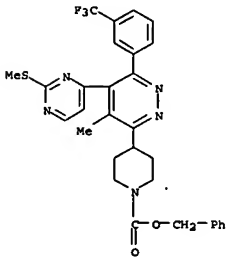
IT **786705-13-3P**, 4-(4-Methyl-5-(2-methylsulfanylpyrimidin-4-yl)-6-(3-trifluoromethylphenyl)pyridazin-3-yl]piperidine-1-carboxylic acid benzyl ester **786705-15-5P**, 4-[5-(2-Methylsulfonylpyrimidin-4-yl)-4-methyl-6-(3-trifluoromethylphenyl)pyridazin-3-yl]piperidine-1-carboxylic acid benzyl ester **786705-17-7P**, 4-[4-Methyl-5-[2-(1-phenylethylamino)pyrimidin-4-yl]-6-(3-trifluoromethylphenyl)pyridazin-3-yl]piperidine-1-carboxylic acid benzyl ester **786705-19-9P**, [4-[5-Methyl-6-(piperidin-4-yl)-3-(3-trifluoromethylphenyl)pyridazin-4-yl]pyrimidin-2-yl](1-phenylethyl)amine **786705-21-3P**, 2-Hydroxy-1-[4-[4-methyl-5-[2-(1-phenylethylamino)pyrimidin-4-yl]-6-(3-trifluoromethylphenyl)pyridazin-3-yl]piperidin-1-yl]propan-1-one **786705-23-5P**, (S)-4-[4-Methyl-5-[2-(1-phenylethylamino)pyrimidin-4-yl]-6-(3-trifluoromethylphenyl)pyridazin-3-yl]piperidine-1-carboxylic acid benzyl ester **786705-25-7P**, [4-[5-Methyl-6-(piperidin-4-yl)-3-(3-trifluoromethylphenyl)pyridazin-4-yl]pyrimidin-2-yl]((S)-1-phenylethyl)amine **786705-27-9P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(TNF and/or IL inhibitor; prepn. of substituted pyridazines and analogs as TNF and IL inhibitors for treatment inflammation, pain, and other disorders)

RN 786705-13-3 CAPLUS

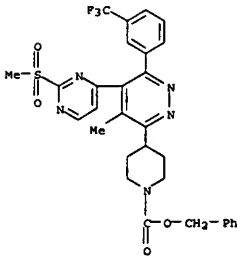
CN 1-Piperidinecarboxylic acid, 4-[4-methyl-5-[2-(methylthio)-4-pyrimidinyl]-6-[3-(trifluoromethyl)phenyl]-3-pyridazinyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 786705-15-5 CAPLUS

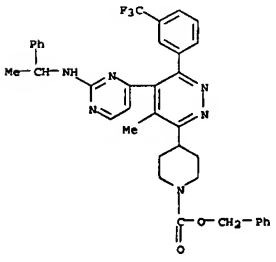
CN 1-Piperidinecarboxylic acid, 4-[4-methyl-5-[2-(methylsulfonyl)-4-pyrimidinyl]-6-[3-(trifluoromethyl)phenyl]-3-pyridazinyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 786705-17-7 CAPLUS

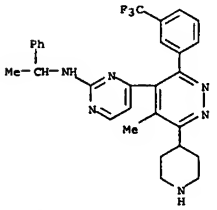
CN 1-Piperidinecarboxylic acid, 4-[4-methyl-5-[2-[(1-phenylethyl)amino]-4-pyrimidinyl]-6-[3-(trifluoromethyl)phenyl]-3-pyridazinyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 786705-19-9 CAPLUS

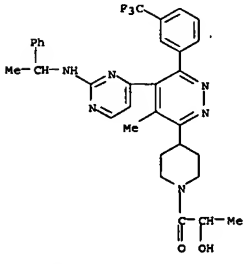
CN 2-Pyrimidinamine, 4-(5-methyl-6-(4-piperidinyl)-3-[3-(trifluoromethyl)phenyl]-4-pyridazinyl]-N-(1-phenylethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 786705-21-3 CAPLUS

CN Piperidine, 1-(2-hydroxy-1-oxopropyl)-4-[4-methyl-5-[2-[(1-phenylethyl)amino]-4-pyrimidinyl]-6-[3-(trifluoromethyl)phenyl]-3-pyridazinyl]- (9CI) (CA INDEX NAME)

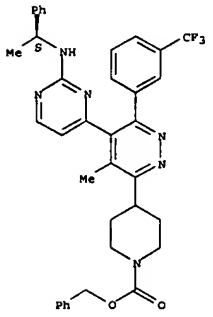


RN 786705-23-5 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[4-methyl-5-[2-[[(1S)-1-phenylethyl]amino]-4-pyrimidinyl]-6-[3-(trifluoromethyl)phenyl]-3-pyridazinyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

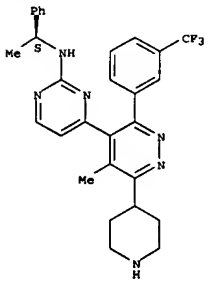
Absolute stereochemistry.

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 786705-25-7 CAPLUS
CN 2-Pyrimidinamine, 4-[5-methyl-6-(4-piperidinyl)-3-[3-(trifluoromethyl)phenyl]-4-pyridazinyl]-N-[(1S)-1-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

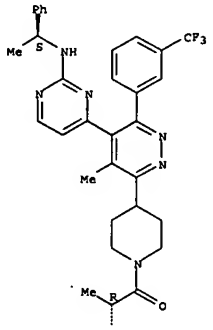


L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

RN 786705-27-9 CAPLUS
CN Piperidine, 1-[(2R)-2-hydroxy-1-oxopropyl]-4-[4-methyl-5-[2-[[(1S)-1-phenylethyl]amino]-4-pyrimidinyl]-6-[3-(trifluoromethyl)phenyl]-3-pyridazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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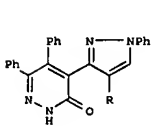
OH

L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:807136 CAPLUS
DOCUMENT NUMBER: 130:95521
TITLE: Synthesis and antimicrobial activity of pyrazolo[3',4':4,3]pyrido[6,5-c]pyridazine and thieno[2,3-c]pyridazine derivatives
AUTHOR(S): El-Dean, Kamal A. M.; Radwan, S. M.
CORPORATE SOURCE: Chemistry Dep., Faculty Science, Assiut Univ., Assiut, 71516, Egypt
SOURCE: Pharmazie (1998), 53(12), 839-843
CODEN: PHARAT; ISSN: 0031-7144
PUBLISHER: Govi-Verlag Pharmazeutischer Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:95521
GI



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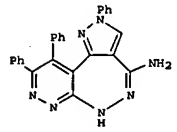

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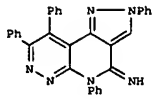


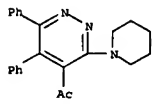
IV

AB 4-Acetyl-5,6-diphenyl-3(2H)-pyridazinone (I) was allowed to react with PhNHNH2 to afford the corresponding hydrazone. Upon treatment with POCl3/DMF, the hydrazone gave pyrazolylpyridazine II (R = CHO), which was allowed to react with thiosemicarbazide and NH2OH to give the corresponding thiosemicarbazone and oxime, resp. Treatment of the oxime with Ac2O gave the carbonitrile II (R = CN). The oxime reacts with POCl3 to give 3-chloro-5,6-diphenyl-4-(4-cyano-1-phenyl-3-pyrazolyl)pyridazine. Subsequent reaction with N2H4.H2O or PhNH2 afforded pyrazolopyridazodiazepine III or pyrazolopyridazopyridazine IV. When I was allowed to react with POCl3, 3-chloro-4-acetyl-5,6-diphenylpyridazine was obtained. This compound reacts with thiourea, N2H4.H2O, or piperidine to give 4-acetyl-5,6-diphenyl-3(2H)-pyridazinethione, one (V), 3-methyl-4,5-diphenyl-(1H)-pyrazolo[3,4-c]pyridazine, and 3-piperidinyl-4-acetyl-5,6-diphenylpyridazine, resp. Compound V reacted with α-halo ester or α-halo ketone to give thienopyridazines. Most of the prepared compds. showed bactericidal activity, and some of

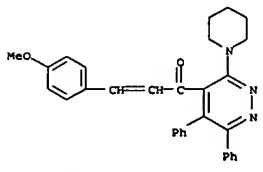
L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

exhibited fungicidal activity.

IT 126679-74-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antimicrobial activity of pyrazolopyridopyridazines and thienopyridazines)
RN 126679-74-1 CAPLUS
CN Ethanone, 1-[5,6-diphenyl-3-(1-piperidinyl)-4-pyridazinyl]- (9CI) (CA INDEX NAME)

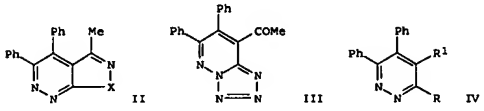


IT 219565-58-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antimicrobial activity of pyrazolopyridopyridazines and thienopyridazines)
RN 219565-58-9 CAPLUS
CN 2-Propen-1-one, 1-[5,6-diphenyl-3-(1-piperidinyl)-4-pyridazinyl]-3-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:198273 CAPLUS
DOCUMENT NUMBER: 112:198273
TITLE: Reactivity of 4-acetyl-3-chloro-5,6-diphenylpyridazine towards some nucleophilic reagents, synthesis of some fused pyridazine derivatives
AUTHOR(S): Ismail, M. Fekry; Sayed, Fekria S.; El-Khamry, Abdel Moemen A.; Ali, M. A.; Mansour, M. M.
CORPORATE SOURCE: Fac. Sci., Ain Shams Univ., Abbassia, Egypt
SOURCE: Journal fuer Praktische Chemie (Leipzig) (1989), 331(3), 399-404
CODEN: JPCEAO; ISSN: 0021-8383
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 112:198273
GI



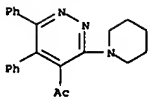
II III IV

AB 4-Acetyl-3-chloro-5,6-diphenylpyridazine (I), prepared by the action of POCl3 on 4-acetyl-5,6-diphenylpyridazin-3(2H)-one, reacts with hydrazine hydrate and phenylhydrazine to give the pyrazolopyridazines II (X = NH, NPh) resp. Reaction of I with hydroxylamine hydrochloride gave the isoxazolopyridazine derivative II (X = O), while its reaction with sodium azide in DMF gave the tetrazolopyridazine III. Primary amines react with I to give either of the amino derivs. IV (R = NHPh, R1 = CMe:NPh; R = NHPh, NHBu, R1 = Ac) depending upon the reaction conditions. Treatment of I with piperidine or morpholine gave I (R = piperidino, morpholino, R1 = Ac) resp. 4-Acetyl-5,6-diphenylpyridazine-3(2H)-thione was readily obtained by the action of thiourea on ethanolic solution of I. The reactions of I with phenols were also investigated.

IT **126679-74-1P 126679-75-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 126679-74-1 CAPLUS
CN Ethanone, 1-[5,6-diphenyl-3-(1-piperidinyl)-4-pyridazinyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 126679-75-2 CAPLUS
CN Ethanone, 1-[3-(4-morpholinyl)-5,6-diphenyl-4-pyridazinyl]- (9CI) (CA INDEX NAME)